

WHAT IS CLAIMED IS:

1 1. A method of chemically ligating two oligopeptides, wherein a first
 2 oligopeptide thioester having an acidic C-terminal amino acid, said acidic C-terminal amino
 3 acid having a thioester moiety, a side chain, and a side chain protecting group such that said
 4 side chain protecting group substantially prevents rearrangements between atoms of said side
 5 chain and atoms of said thioester moiety, is contacted with a second oligopeptide having an
 6 N-terminal amino acid under chemical ligation conditions such that said thioester moiety of
 7 said first oligopeptide thioester ligates to said N-terminus of said second oligopeptide to form
 8 an oligopeptide or polypeptide product.

1 2. The method of claim 1 wherein said side chain protecting group is
 2 selected from the group consisting of 9-fluorenylmethyl ester, (phenylsulfonyl)ethyl ester,
 3 2,2,2-trichloroethyl ester, and a phenacyl ester.

1 3. The method of claim 2 wherein said side chain protecting group is a
 2 phenacyl ester having the formula:



4 wherein R^{13} and R^{14} are each electron-donating groups.

1 4. The method of claim 3 wherein R^{13} and R^{14} are each alkyl having from
 2 1 to 3 carbon atoms.

1 5. The method of claim 4 wherein R^{13} is methyl or ethyl.

1 6. The method of claim 2 wherein said N-terminal amino acid of said
 2 second oligopeptide is cysteine or an amino acid with a removable ethylthiol moiety.

1 7. The method of claim 1 wherein one of said first and second
 2 oligopeptide is attached to a solid support.

1 8. An oligopeptide thioester defined by the formula:



3 wherein:

4 each Xaa_i is independently a protected or unprotected amino acid for $i=1$ to m ;
 5 m is an integer from 2 to 70;

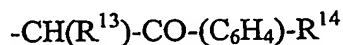
n is an integer equal to 1 or 2;

R¹¹ is a member selected from the group consisting of alkyl having from 1 to 6 carbon atoms, alkylaryl having from 6 to 8 carbon atoms, -CH₂-CONH₂, -CH₂CH₂CONH₂, and -(CH₂)_k-CO-Xaa, wherein subscript k is an integer equal to 1 or 2 and Xaa is an amino acid; and

R¹² is a carboxy protecting group.

9. The oligopeptide of claim 8 wherein R¹² is selected from the group consisting of 9-fluorenylmethyl ester, (phenylsulfonyl)ethyl ester, 2,2,2-trichloroethyl ester, and a phenacyl ester.

10. The oligopeptide of claim 9 wherein R¹² is a phenacyl ester defined by the formula:



wherein R¹³ and R¹⁴ are each an electron-donating group.

11. The oligopeptide of claim 8 wherein said oligopeptide thioester is attached to a solid support.